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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,225	09/26/2003	Ivan Alferiev	RCHP-125US1	2873
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			ART UNIT 1641	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary**Application No.**

10/672,225

Applicant(s)

ALFERIEV ET AL.

Examiner

David J. Venci

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 17, 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-31 is/are pending in the application.
- 4a) Of the above claim(s) 4,8-13,15,17,21 and 23-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-7,14,16,18-20 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-31 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 17, 2008, has been entered.

Claims 23-30 are drawn to a nonelected invention and were withdrawn from further consideration pursuant to 37 CFR 1.142(b) in the Office Action dated December 8, 2006. Claims 4, 8-13, 15, 17 and 21 are drawn to nonelected species and were withdrawn from further consideration pursuant to 37 CFR 1.142(b) in prior Office Action.

In prior Office Action, claim 18 was withdrawn from consideration pursuant to 37 CFR 1.142(b) for allegedly being drawn to a nonelected species. In response, Applicants argue that claim 18 is directed to a "reactive moiety" as depicted in Fig. 2 of the specification (see Applicants' reply p. 7 of 11, first paragraph). Applicants' argument appears persuasive and, accordingly, claim 18 is rejoined.

Claims 12 and 13 appear to be directed to non-elected species and were withdrawn from further consideration pursuant to 37 CFR 1.142(b) in the Office Action dated July 11, 2007.

Currently, claims 1-3, 5-7, 14, 16, 18-20 and 22 are under examination.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness^{1,2} rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-3, 5-7, 14, 16, 19, 20 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pope & Knigge (US 5,399,501) in view of Melancon (US 4,922,113).

Pope & Knigge describe a method of preparing a surface for binding capacity determination, the method comprising the following claimed steps:

1. providing a surface comprising a first reactive moiety (see col. 4, lines 26-32, "B is a solid phase having an amino, carboxyl or thiol group");
2. contacting the surface with a fluorophore comprising a second reactive moiety, thereby causing a reaction between the first and second reactive moieties (see Abstract, sixth sentence, "the solid phase is reacted with a disulfide compound to form a complex"; see e.g., col. 7, line 50, "N,N'-didansyl-L-cystine"), and forming a linking bond that binds the fluorophore to the surface (see Abstract, sixth sentence, "form a complex");

¹ In the Supreme Court decision *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), the Court set forth factual inquiries establishing a background for determining obviousness under 35 U.S.C. 103(a). The factual inquiries include: (1) determining the scope and contents of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the pertinent art; and (4) considering objective evidence indicating obviousness or nonobviousness.

² The lack of objective evidence of nonobviousness in the instant application does not suggest "the level of ordinary skill in the pertinent art" is high.

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3. cleaving the linking bond, thereby liberating the fluorophore from the surface (see Abstract, sixth sentence, "the complex is reacted with a reductant"; see *e.g.*, Fig. 6, noting the liberation of $-S-R'$ from the surface after the second reaction);

Pope & Knigge do not teach steps of "exposing" liberated fluorophore to exciting radiation, "measuring" fluorescence from the liberated fluorophore, or "calculating" binding capacity.

However, Melancon describe the claimed steps:

4. exposing the liberated fluorophore to exciting radiation (see Abstract step b, "scanning the coating with radiant energy having a wavelength within wavelength λ_1 ";
5. measuring fluorescence from the liberated fluorophore (see Abstract, step c, "detecting the radiant energy of wavelength λ_2 emitted by the coating")
6. calculating binding capacity (see Abstract, step d, "correlating the emitted radiant energy to independently measured standard coating weights or thicknesses")

It would have been obvious to a person of ordinary skill to monitor Pope & Knigge's method using fluorescence because Melancon reiterates that, in addition to correlating fluorescence to binding capacity (*i.e.*, "coating weights or thicknesses"), fluorescence measurements also allow detection of coat uniformity and defects (see Abstract).

With respect to claims 2 and 3, Pope & Knigge describe a method wherein the linking bond is a disulfide bond that is subsequently cleaved (see col. 4, lines 39-43, "form a solid phase/disulfide complex which is then reacted with a reductant, whereby the disulfide is reduced to form a thiolated solid phase").

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With respect to claims 5-7, Pope & Knigge describe dansyl-cysteine (see col. 7, line 50).

With respect to claim 14, Pope & Knigge describe surfaces made of polymer (see col. 6, lines 33-34, "polymeric"), metal (see col. 6, line 41, "alumina"), biomaterial (see col. 6, line 38, "polysaccharides") and semiconductor (see col. 6, line 40, "silicon particles").

With respect to claim 16, Pope & Knigge describe a method wherein the surface comprises a first reactive "thiol" moiety (see col. 4, lines 26-32, "B is a solid phase having an amino, carboxyl or thiol group").

With respect to claim 19, Pope & Knigge describe a method wherein the surface comprises a reactive dithio group (see Fig. 4, —S—X—SH).

With respect to claim 20, Pope & Knigge describe a method incorporating reducing agents such as borohydrides (see col. 9, line 42) or dithiothreitol (see col. 10, lines 4-5).

With respect to claim 31, Pope & Knigge describe a method incorporating a step of washing the surface (see col. 15, line 46-50, "A second aliquot of 5 mg EDC in 0.5 ml deionized water was added, and the suspension was rotated... centrifuged, and the supernatant was discarded") (paraphrasing mine), which effectively removes unbound reactants.

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Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pope & Knigge (US 5,399,501) and Melancon (US 4,922,113) as applied to claims 1, 2 and 20, and further in view of Burns *et al.*, 56 J. ORG. CHEM. 2648 (1991).

Pope & Knigge and Melancon describe a method of determining a binding capacity of a surface as substantially described, *supra*, and incorporated herein.

Pope & Knigge and Melancon do not describe a tris(2-carboxyethyl)phosphine (hereinafter "TCEP") reducing agent.

However, Burns *et al.* describe the general use of TCEP for selective reduction of disulfides (see Title).

It would have been obvious for a person of ordinary skill in the art to modify the method of Pope & Knigge and Melancon by using TCEP because Burns *et al.* discovered that TCEP reduces disulfides "rapidly and completely" at acidic pH (see Abstract), said acidic pH being necessary to prevent thiolate-disulfide interchange (see p. 2649, col. 1, last paragraph).

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Claim 1-3, 14, 16, 18-20 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clark & Pai (WO 96/07676) in view of Melancon (US 4,922,113).

Clark & Pai describe a method of preparing a surface for binding capacity determination, the method comprising the following claimed steps:

1. providing a surface comprising a first reactive moiety (see paragraph bridging pp. 3-4, "solid synthetic resin");
2. contacting the surface with a fluorophore comprising a second reactive moiety, thereby causing a reaction between the first and second reactive moieties, and forming a linking bond that binds the fluorophore to the surface (see paragraph bridging pp. 33-34, "The resin was recoupled overnight with DTNB");
3. cleaving the linking bond, thereby liberating the fluorophore from the surface (see paragraph bridging pp. 33-34, "200 mg of DTNB resin was added to 2 ml of NMP containing 1 millimole of DTT... supernatant turned pink");

Clark & Pai do not teach steps of "exposing" liberated fluorophore to exciting radiation, "measuring" fluorescence from the liberated fluorophore, or "calculating" binding capacity.

However, Melancon describe the claimed steps:

4. exposing the liberated fluorophore to exciting radiation (see Abstract step b, "scanning the coating with radiant energy having a wavelength within wavelength λ_1 ");

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5. measuring fluorescence from the liberated fluorophore (see Abstract, step c, "detecting the radiant energy of wavelength λ_2 emitted by the coating")
6. calculating binding capacity (see Abstract, step d, "correlating the emitted radiant energy to independently measured standard coating weights or thicknesses")

It would have been obvious to a person of ordinary skill to monitor Clark & Pai's method using fluorescence because Melancon reiterates that, in addition to correlating fluorescence to binding capacity (*i.e.*, "coating weights or thicknesses"), fluorescence measurements also allow detection of coat uniformity and defects (see Abstract).

With respect to claim 14, Clark & Pai describe surfaces made of polymer (see paragraph bridging pp. 3-4, "polyolefins"), biomaterial (see paragraph bridging pp. 3-4, "natural product") or ceramic (see paragraph bridging pp. 3-4, "controlled pore glass").

With respect to claim 16, Clark & Pai describe a method wherein the surface comprises a first "thiol-reactive" moiety (see p. 3, Formulas I and II).

With respect to claims 18 and 19, Clark & Pai describe a method wherein the surface comprises a dithiol reaction product of a surface thiol with DTNB (see Table I, Disulfide Resin Nos. 1, 2, 3, 5, 6 and 7).

With respect to claim 20, Clark & Pai describe a method wherein the step of "cleaving" is accomplished with dithiothreitol (see p. 34, middle of page).

With respect to claim 31, Clark & Pai describe a method incorporating a step of washing the surface (see p. 34, lines 5-7, "washed twice"), which effectively removes unbound reactants.

Response to Arguments

Claim Rejections - 35 USC § 112

In prior Office Action, claim 1 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the consecutive steps of "contacting" thereby "forming" a linking bond immediately followed by "cleaving the linking bond" was considered unclear.

In response, Applicants point to the specification sentence bridging pp. 12-13, which teaches performing a "washing" step between the steps of "contacting" and "cleaving". Applicants' argument is persuasive insofar as the claimed method corresponds to the method taught in the specification sentence bridging pp. 12-13.

Claim Rejections - 35 USC § 103

In prior Office Action, claims 1-3, 5-7, 14, 16, 19 and 20 were rejected under 35 U.S.C. 103(a) as being unpatentable over Pope & Knigge (US 5,399,501) in view of Melancon (US 4,922,113).

In response, Applicants argue:

1. Pope & Knigge do not disclose the claimed step of "calculating" binding capacity.
2. Neither Pope & Knigge nor Melancon disclose a "liberated" fluorescent moiety.

Applicants' arguments have been carefully considered but are not persuasive.

With respect to 1), Examiner relies upon the teachings of Melancon for the claimed step of "calculating" binding capacity (see Melancon, Abstract, step d, "correlating the emitted radiant energy to independently measured standard coating weights or thicknesses"). It would have been obvious for persons of ordinary

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skill to incorporate Melancon's "calculating" steps into Pope & Knigge's method because Melancon affords Pope & Knigge the opportunity to monitor coat uniformity and defects during preparation of their binding assay surfaces.

With respect to 2), Applicants' claimed invention requires performing nothing more than "cleaving... thereby liberating" (see claim 1, step 3). Contrary to that suggested in Applicants' reply, Applicants' claimed invention does not require a "supernatant" resulting from performing one or more "separating" or "purifying" steps (see Applicants' reply, p. 8 of 11, last sentence). Thus, Pope & Knigge's description of linking bond "cleaving" (see Pope & Knigge, Abstract, sixth sentence, "the complex is reacted with a reductant"; see e.g., Fig. 6, noting the liberation of $-S-R'$ from the surface after the second reaction) fully describes the claimed fluorophore "liberated" from its surface.

Conclusion

No claims are allowable at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is (571)272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on 571-272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Assistant Examiner
Art Unit 1641

/dv/

/Mark L. Shibuya/
Supervisory Patent Examiner, Art Unit 1641